



NOTES

DIABETES MELLITUS

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- A group of chronic disorders characterized by abnormal glucose metabolism resulting in elevated blood glucose levels

CAUSES

- Genetic predisposition, lifestyle factors

COMPLICATIONS

- Hyper/hypoglycemia, diabetic ketoacidosis, hyperosmolar hyperglycemic state (HHS), vascular and neurological pathology, renal disease

SIGNS & SYMPTOMS

- Symptomatic hyperglycemia

DIAGNOSIS

LAB RESULTS

Urinalysis

- Albuminuria, glycosuria

Blood tests

- ↑ Non-fasting/fasting glucose tests
- ↑ HbA_{1c}
- Diabetic ketoacidosis (DKA)
 - Glucose > 250mg/dL
- Hyperosmolar hyperglycemic state (HHS)
 - Glucose > 600mg/dL

OTHER DIAGNOSTICS

Physical examination

- Fundoscopic exam
 - Cotton wools spots, flare hemorrhages
- Monofilament testing
 - ↓ sensation
- Lower extremities
 - ↓ pedal pulses, presence of ulcers

TREATMENT

MEDICATIONS

- Diabetes mellitus type I
 - Insulin
- Diabetes mellitus type II
 - Oral antidiabetic agents, insulin

OTHER INTERVENTIONS

- Metabolism regulation with diet
- Weight loss, exercise
- Smoking cessation

VISIT...

LANZAROTE
Caliente.COM

DIABETES MELLITUS TYPE 1

osms.it/diabetes-mellitus-type-1

PATHOLOGY & CAUSES

- Chronic metabolic disease; destroys **pancreatic beta cells** → insulin deficiency, hyperglycemia
- Diabetes (going through) mellitus (honey/sweet)
- ↓ insulin → glucose unable to enter cells → hyperglycemia
 - Cells “starve” due to no glucose for energy generation → polyphagia, fatigue
 - Glucose exceeds renal threshold → glycosuria → **osmotic diuresis** → polyuria → hypovolemia
 - ↑ serum osmolality + hypovolemia → polydipsia
 - Endothelial glycosylation (endothelial cells unable to downregulate glucose transport in setting of extracellular hyperglycemia) → damage to endothelial cells → microvascular damage + accelerated atherosclerosis in large vessels
 - Narrowing of vascular lumens → ↓ microcirculation → tissue ischemia, cellular loss
 - ↓ blood supply to nerves → segmental demyelination → slowing of nerve conduction neuropathy

TYPES

Type 1A: immune-mediated diabetes

- Most common
- Autoimmune destruction of pancreatic beta-cells
- Type IV hypersensitivity response

Type 1B: idiopathic diabetes

- No evidence of autoimmunity
- Varying degrees of low insulin, episodes of ketoacidosis

Latent autoimmune diabetes

- Progressive form of autoimmune diabetes
- Onset at > 30 years old

RISK FACTORS

- Genetic predisposition
- Multiple gene polymorphisms associated with DM Type I
 - HLA-DQalpha, HLA-DQbeta, HLA-DR, PTPN22 gene, CTLA-4

COMPLICATIONS

- ↑ risk of infection, delayed wound healing; ↑ risk of amputations
- Diabetic ketoacidosis
 - Hyperglycemia (> 250mg/dL), ketonemia, metabolic acidosis
- Neuropathy
 - Autonomic, somatic

Microvascular

- **Retinopathy**, nephropathy, erectile dysfunction

Macrovascular

- **Cardiovascular**, cerebrovascular, and peripheral vascular disease

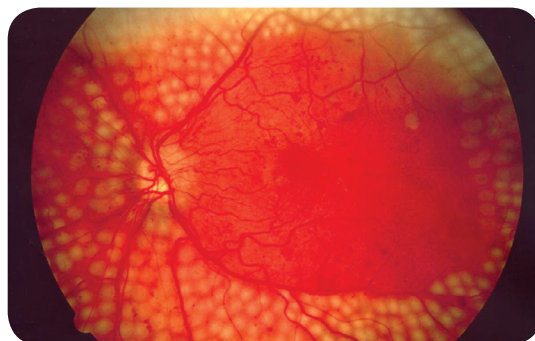


Figure 14.1 A retinal photograph of an individual who has received laser treatment for proliferative retinopathy as a consequence of diabetes mellitus.



Figure 14.2 An individual with diabetes mellitus and charcot arthropathy of the left ankle. Lack of sensation to the joint causes results in repetitive microtrauma which eventually leads to bony destruction and joint malformation.

SIGNS & SYMPTOMS

- **Classic presentation:** polyuria, polydipsia, polyphagia (3Ps)
 - Dehydration → dry mucous membranes/decreased skin turgor
- Fatigue, lethargy
- Blurred vision
- Gastroparesis → constipation
- Paresthesias
- Unexplained weight loss
- **Mild hyperglycemia**, may be asymptomatic
- **Volume depletion:** symptomatic moderate to severe hyperglycemia
 - Dry mucous membranes, hypotension, poor skin turgor

DIAGNOSIS

LAB RESULTS

Non-fasting/random glucose test

- 200mg/dL

Fasting glucose test

- Prediabetes: 110–125mg/dL
- Diabetes: ≥ 126 mg/dL

HbA1c glycated hemoglobin test

- Indicates glucose level control over prolonged period
- Prediabetes: 5.7–6.4% HbA1c
- Diabetes: $> 6.5\%$ HbA1c

Urinalysis

- Albuminuria, glycosuria

Differentiation from Type II diabetes

- **Autoantibodies against beta cells:** glutamic acid decarboxylase autoantibodies (GADA), insulinoma-associated-2 autoantibodies (IA-2A), islet cell autoantibodies, insulin autoantibodies (IAA), zinc transporter 8 (ZnT8Ab)
- C-peptide: insulin low

OTHER DIAGNOSTICS

Physical examination

- **Fundoscopy exam:** cotton wools spots, flare hemorrhages
- **Monofilament testing:** ↓ sensation
- **Lower extremities:** ↓ pedal pulses, presence of ulcers



Figure 14.3 A neuropathic ulcer on the heel of an individual with diabetes mellitus.

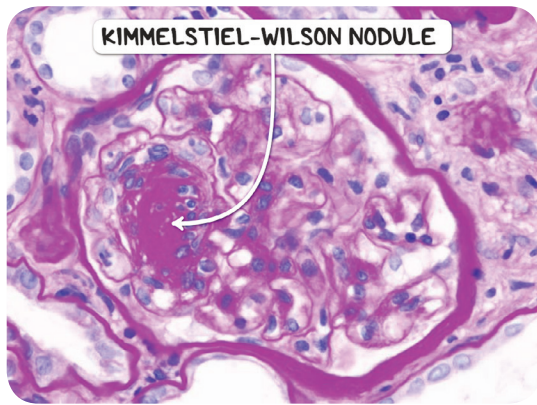


Figure 14.4 The histological appearance of a glomerulus in an individual with diabetes mellitus. The glomerular basement membrane is thickened and there is mesangial proliferation leading to the appearance of a Kimmelstiel–Wilson nodule.

TREATMENT

MEDICATIONS

- Lifelong **insulin** therapy (short-acting insulin/insulin pump)

DIABETES MELLITUS TYPE II

osms.it/diabetes-mellitus-type-2

PATHOLOGY & CAUSES

- Metabolic disorder; varying degrees of resistance to insulin
- Most common type of diabetes in adults (90–95%)

CAUSES

- Insulin resistance (inherited, acquired) → beta cell hyperplasia, hypertrophy → ↑ beta cell secretion of insulin + amylin production → hyperinsulinemia, amyloid deposits within beta cells → beta cell exhaustion, dysfunction, atrophy → ↓ insulin production → hyperglycemia
- Genetic polymorphisms associated with DM Type II
 - TCF7L2, GCK, HNF1B, WFS1, KCNJ11, PPARG, IRS1

RISK FACTORS

- Multifactorial; interaction between genetic, environmental, behavioral factors

- Family history, physical inactivity, poor diet, obesity, > 45 years old, history of gestational diabetes, prediabetes, polycystic ovary syndrome (PCOS), medications that adversely affect glucose tolerance/↑ blood glucose levels (e.g. glucocorticoids, atypical antipsychotics, thiazide diuretics)

COMPLICATIONS

- ↑ risk of **cardiovascular**, peripheral artery disease

Hyperosmolar hyperglycemic state (HHS)

- Profound hyperglycemia (>600mg/dL) → ↑ plasma osmolarity (>320mOsm/kg) → systemic, cellular dehydration
- Mental status changes; thrombotic events; polyuria; mild ketonemia, acidosis; high mortality rate

SIGNS & SYMPTOMS

- Polyuria, polydipsia, polyphagia; glycosuria, weakness, unexplained weight loss, blurred vision; acanthosis nigricans (hyperpigmented cutaneous patches) related to insulin resistance

DIAGNOSIS

LAB RESULTS

Non-fasting/random glucose test

- 200mg/dl

Fasting glucose test

- Prediabetes: 110–125mg/dl
- Diabetes: 126mg/dl

Oral glucose tolerance test

- Prediabetes: 99–140mg/dl
- Diabetes: ≥ 200

HbA_{1c} glycated hemoglobin

- Prediabetes: 5.7–6.4%
- Diabetes: $> 6.5\%$

Differentiation from Type I

- Autoantibodies
 - Absent
- C peptide
 - Normal/elevated

OTHER DIAGNOSTICS

Physical examination

- Fundoscopic exam: cotton wool spots, flare hemorrhages
- Monofilament testing: $\downarrow$ sensation
- Lower extremities: $\downarrow$ pedal pulses, presence of ulcers

TREATMENT

MEDICATIONS

- Metformin; sulfonylureas, meglitinides
- Long/short-acting insulin

OTHER INTERVENTIONS

- Weight loss, exercise, diet management

DIABETIC KETOACIDOSIS

osms.it/diabetic-ketoacidosis

PATHOLOGY & CAUSES

- Medical emergency due to cell starvation $\rightarrow$ altered mental status
- Arises with stress/infection, individuals with poorly regulated glucose levels
- Epinephrine $\rightarrow$ glucagon $\rightarrow$ lipolysis $\rightarrow$ free fatty acids $\rightarrow$ ketone bodies, acetoacetic, hydroxybutyric acid $\rightarrow$ $\uparrow$ blood acidity
- Occurs in Type I, long-standing Type II DM when body completely stops producing insulin

COMPLICATIONS

- Acute cerebral edema
 - High glucose $\rightarrow$ osmotic shift of water to extracellular fluid
- Hyperkalemia due to H⁺/K⁺ exchange mechanisms in regulating acidosis $\rightarrow$ arrhythmias

RISK FACTORS

- Infection, stress, irregular insulin use

SIGNS & SYMPTOMS

- Anion gap metabolic acidosis, bicarbonate low → insulin stops letting potassium into cells, potassium acts as buffer by letting hydrogen into cells → **hyperkalemia** → ultimately lost in urine
- **Dehydration** (individual extremely thirsty), nausea, vomiting, mental status change
- **Kussmaul respiration**
 - Deep, labored breathing to move carbon dioxide out of blood
- **Acetone breath**
 - Ketone bodies break down into acetone → excrete as gas through lungs

DIAGNOSIS

LAB RESULTS

- **Hyperkalemia** ($> 5.2\text{mg/dl}$), initially with hypokalemia ($< 3.5\text{mg/dl}$)
- Glucose $> 250\text{mg/dL}$

Acid base status

- Ketones present in urine; arterial gas, bicarbonates measured; $\text{pH} < 7.3$

TREATMENT

MEDICATIONS

Insulin

- Lower blood glucose
- Monitor carefully
 - Rapid decrease in serum glucose → osmotic shift of water intracellularly → risk for cerebral edema → increased ICP
- Treat cerebral edema with hypertonic solution (3% saline, mannitol)

Fluid, electrolyte replacement

- 0.9% normal saline + potassium (KCl); serum K^+ levels drop as insulin shifts potassium intracellularly → risk for hypokalemia
- Bicarbonates
 - Reverse acidosis

OTHER INTERVENTIONS

- Fluids, rehydration